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Despite the fact that approximately 43% of all breast cancers occur in women over 70 years of age, no previous randomized controlled trial (RCT) addressed women in this age group. Without clear evidence, the usefulness of the mammograms currently performed on 15-36% of women over age 70 is unknown.

We present the use of an administrative utilization database linked to breast cancer outcomes to examine the usefulness of mammography in women age 70 and older. Using the Linked Medicare-SEER Tumor Registry Database, created by the National Cancer Institute and the Health Care Financing Administration, we have created a database of 9767 women diagnosed with breast cancer from January 1, 1987 to December 31, 1993, and compared mammography users versus nonusers on stage of presentation, all cause survival and breast cancer survival.

Women over 70 years who were nonusers of mammography were diagnosed with breast cancer at Stage II or greater more often than regular users (adjusted odds ratio (OR), 3.12 [95% CI, 2.74-3.58]). Nonusers of mammography were at significantly greater risk of dying from their breast cancer than regular users for all women (adjusted hazard ratio (HR), 3.38 [95% CI, 2.65-4.32]) and for women within each age group. Even assuming a lead-time of 1.25 years, nonusers of mammography continued to be at increased risk of dying from breast cancer.

We are currently simulating a case-control study using propensity scores and instrumental variables as an innovative methodology to analyze our data. We hope to demonstrate whether a broad range of methodologies all point to the benefit of screening mammography in older women.

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FOREWORD

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(4) TABLE OF CONTENTS:

(5) INTRODUCTION

Randomized clinical trials

Breast cancer is the second leading cause of cancer-related mortality among women in the United States. Women ages 65 and older bear the greatest burden of disease accounting for more than 43% of newly diagnosed cases of breast cancer (1). Older women are also more commonly diagnosed with advanced stage disease (1-4) and their breast cancer mortality rate s eight times greater than women under age 65 (5). The role of screening mammography in reducing morbidity and mortality from breast cancer in older women is unknown. Randomized controlled trials (RCTs) are inadequate to judge the efficacy of mammography screening, as they did not include sufficient women over age 69 years.

In our last annual report, we presented our methodology to date and data of retrospective cohort study of 9767 women ages 67 and older with breast cancer, diagnosed and staged from 1987 to 1993, in three geographic areas to estimate benefits from prior mammography use for women aged 67–74, 75–84 and 85 and older. Since our last annual report, we have addressed the following technical objectives:

Technical Objective 5:

Task 1 Completed the literature review to identify results form RCTs. Given the lack of data for comparison in the published literature, plan to contact all trial investigators for unpublished data.

Task 2 Due to the lack of available data for comoparison from the randomized clinical trials, we have reviewed the literature on alternative approaches for the evaluation of observational data. We have developed an innovative methodology, utilizing propensity scores and operational variables to address the issues of the use of observational data to address the benefits of mammograpy screening in women over age 70.

Task 3 We have completed our first manuscript, which is in press in the Journal of the American Geriatric Society. The data from our study was presented in both poster format and as an oral presentation in G.S. 1 Novel Approaches to the Early Detection of Breast Cancer at the Era of Hope Department of Defense Breast Cancer Research program Meeting on June 8 – 11, 2000.

We have requested and have received a no-cost extension to complete our revised analysis plan.

(5.1) Background

Mammography Use in Older Women

Early detection with mammography has been consistently shown to decrease breast cancer-related mortality by 30% for women age 50-69 years (6-10). Despite this striking reduction in mortality for women age 50-69, there are currently no data to make a statement about the utility of mammography for women age 70 and older. Although one RCT (The Swedish Two County Trial) included women up to age 74 years, there was inadequate power to detect a difference over age 69 years.

There are reasons to expect that older women would benefit from regular mammography despite the lack of scientific data to establish a benefit. First, mammography is a more specific and sensitive test as women age (11,12). Second, the biology of breast cancer in older women is thought to be similar to women age 50-69 years (13). Third, survival times for older women are sufficiently long to benefit from early detection (14,15). Fourth, the cost effectiveness ratio of breast cancer prevention in the elderly is in a reasonable range (16,17).

Given the lack of scientific data on the usefulness of mammography in women age 70 and older, current practice recommendations vary. Annual mammography is recommended by the American Cancer Society (13) and the American Medical Association Council on Scientific Affairs (18) for women after age 50 with no upper age limit. Annual to biennial mammography is recommended for women age 50-74 by the U.S. Preventive Services Task Force (19). The Task Force does not recommend mammography beyond age 74 (19). Annual mammography is recommended for women age 65-74 by the Forum on Breast Cancer Screening in Older Women. The Forum also suggests that mammography "should be encouraged" at regular intervals of approximately every two years for women age 75 and older whose general health and life expectancy are good (20).

Breast Cancer Survival in Older Women

There are several potential explanations for why older women experience poor breast cancer survival. These include suboptimal use of breast cancer screening, advanced stage at diagnosis, less aggressive workup, and more conservative therapy.

A series of national surveys (Behavioral Risk Factor Surveillance System, Mammography Attitudes and Usage Study, National Health Interview Survey) have documented that mammography use decreases with advancing age (11,21,22). In 1993, only 25% of women age 65 and older on Medicare had at least one mammogram.23 Rates of mammography utilization among women age 65-74, 75-84 and 85+ years were 32%, 21%, and 7%, respectively (23). Factors other than age that influence mammography use in older women include race, income, education, and state of residence (24,25) However, having a regular provider is the most important determinant of mammography use (26-28). We examined mammography utilization among women age 65 and older and found that these sociodemographic factors remained independent predictors of mammography use even after accounting for use of primary care (29).

The stage of breast cancer at diagnosis is the most important predictor of prognosis. Women who are diagnosed while their cancer is localized to the breast experience better 5-year relative survival rate as compared with women diagnosed with more advanced disease (90% versus 64%, respectively) (13). Older women are more likely to be present with advanced disease and are more likely to go unstaged as compared with younger women disease (13,23). Furthermore, age is an independent predictor of advanced stage disease even after adjusting for other important factors (race, marital status, income, education, and source of care) (30-34).

Age has been shown to influence the diagnostic evaluation and treatment offered for breast cancer (35-38). Older women are less likely to receive diagnostic valuations as complete or treatment as aggressive as compared with younger women. However, the poor survival experienced by the older women can primarily be attributed to their advanced stage at diagnosis since stage-specific survival is similar in all age groups and age-related treatment differences do not appear to affect survival (39).

(6) BODY

(6.1) Methods

(6.11) Data Source:

We conducted a retrospective cohort study using the Linked Medicare-Tumor Registry Database (40). The linked database was jointly created by the National Cancer Institute (NCI) and the Health Care Financing Administration (HCFA) to enable researchers to conduct cancer-related health services research. The linked database contains cancer information on patients 65 years of age and older from NCI's SEER Program and Medicare enrollment and utilization information from HCFA's Medicare Statistical System. The linked database contains Medicare data from 1985 to 1994 for breast cancer cases diagnosed between 1973 and 1993.

Two Medicare utilization files are included in the linked database. First is the Medical Provider Analysis and Review (MEDPAR) file, which is a 100 percent utilization file with one record for every inpatient hospitalization or skilled nursing facility stay covered under Medicare Part A. Second is the Physicians' Claims file which is a 100 percent utilization file with one record for every physician claim covered under Medicare Part B. Before 1991, the 100 percent Physicians' Claims file was available for only ten states. Therefore, for our study years, 1987 to 1993, data from the SEER and Medicare Programs overlap in tumor registries for three areas: Connecticut, metropolitan Atlanta, Georgia, and Seattle-Puget Sound, Washington. Specific information describing the linkage between SEER and Medicare has been published elsewhere (40). The match rates for Connecticut, Atlanta, and Seattle were 93.3%, 94.1%, and 91.5%, respectively.

(6.12) Study Sample

Women were eligible for the study sample (n=11,399) if they received a first primary diagnosis of breast cancer between 1 January 1987 and 31 December 1993, were 67 years of age or older, and resided in Connecticut, Atlanta, or Seattle-Puget Sound. Although we selected these areas because physicians' claims were available for all cases, they also represent a geographically diverse population of older women with breast cancer. Women who were enrolled in a health maintenance organization and those with less than two full years of Medicare Part B coverage were not eligible for this study, since their physician claims data (which are required for identifying mammography use) were not available. We restricted our final study sample to women who were 67 years of age and older to ensure that all women had a full two years of Medicare utilization (claims) information before their breast cancer was diagnosed.

(6.13) Measures

We ascertained the following sociodemographic information from SEER: age at diagnosis, marital status, and SEER area. Age at diagnosis (range, 67-107 years) was categorized as 67 to 74, 75 to 84, and 85 and older. Marital status was defined as married or not at diagnosis. SEER area was classified according to the tumor registry of diagnosis: Connecticut, Atlanta, or Seattle. We used 1990 U.S. Census data to define an ecological measure of socioeconomic status: women were assigned to the median household income of their zip code of residence and grouped as $< \$25{,}000$ or $\geq \$25{,}000$.

We obtained information on race from the Medicare beneficiary enrollment file. Enrollees are classified in Medicare files as Black, White, Asian, Native American, Hispanic, or unspecified. We grouped women who were of racial/ethnic backgrounds other than Black or White together because there were too few women to permit separate analyses.

We computed a modified Charlson Comorbidity Index using Deyo's method of classifying ICD-9-CM *(International Classification of Diseases, 9th revision, Clinical Modification)* diagnosis codes from inpatient claims (41). For each woman, we identified all inpatient hospitalizations beginning two years prior to diagnosis and ending one month after diagnosis. A priori, we extended the observation period to one month past diagnosis because we expected women to have at least one hospitalization around the time of diagnosis. We classified women as 1) non-hospitalized (i.e., comorbidity could not be assessed), 2) having no comorbid conditions (Charlson Index of 0), or 3) having one or more comorbid conditions (Charlson Index ≥ 1).

We measured mammography utilization using Medicare physicians' claims. We identified all bilateral mammograms [CPT *(Physicians' Current Procedural Terminology)* procedure codes 76091 *(mammography, bilateral)* or 76092 *(screening mammography, bilateral, two films each breast)*] within two years prior to the breast cancer diagnosis. We classified women as 1) *nonusers* (n=2,029) if they had no mammograms during the entire two year period prior to diagnosis, 2) *regular users* (n=2,383) if they had at least two mammograms within the two years prior to their breast cancer diagnosis that were ten or more months apart, and 3) *peri-diagnosis users* (n=5,355) if they had their only mammogram(s) within three months before diagnosis. The peri-diagnosis users were a heterogeneous group of women whose

only mammography use was close to their breast cancer diagnosis. This group includes women who had a screening mammogram which led to their breast cancer diagnosis and those whose mammograms were diagnostic. Therefore, analyses relating prior mammography use to breast cancer outcomes considered only nonusers and regular users, as they are clearly distinct groups.

Our first outcome was stage at diagnosis. We developed measures of cancer stage using both the Historical Staging System, and the TNM (tumor, node, metastases) staging system adopted by the American Joint Committee on Cancer. We utilized the latter system as the one most universally used, and providing a greater degree of differentiation across stages. The disadvantage is that we had to drop an additional 844 patients from analyses who did not have this information. We categorized late-stage disease using two classification schemes. First, women diagnosed with carcinoma in situ or Stage I tumors were classified as early-stage; those diagnosed with Stage II or greater tumors were classified as having late-stage disease. Second, we restricted late-stage disease to include only women diagnosed with Stage IIB or greater; women diagnosed with Stage IIA were reclassified as having had early-stage disease. We repeated our analyses using both classification systems and obtained similar results. We present our analyses classifying late-stage disease as Stage II or greater because they provide a more conservative estimate of the mammography-stage association.

Our second outcome was breast cancer mortality among women with invasive tumors. Women who had carcinoma in situ (n=479) were excluded from this analysis because it is unknown which tumors will progress to invasive disease. We measured survival time as the number of days from date of diagnosis until date of death or 31 December 1994 (end of follow-up). Date of death was obtained from the 1994 Medicare beneficiary enrollment file. Cause of death, obtained from SEER, captures the underlying cause listed on the death certificate. Women who had ICD-O *(International Classification of Diseases, Oncology)* codes 174.8 and 174.9 were classified as having died from breast cancer. We also calculated and present all cause mortality.

Women whose mammography use could not be categorized (788 women) or whose disease was unstaged (844 women) were excluded from the study. Overall, there were 741 women age 67 to 74 years, 620 women 75 to 84 years, and 271 women 85 and older who met these exclusion criteria.

Follow-up for our final sample (n=9,767) ranged from one to eight years depending on the year of diagnosis. By the end of 1994, 2,332 deaths had occurred; 889 deaths were attributed to breast cancer (385 women 67 to 74 years, 390 women 75 to 84 years, and 114 women 85 years and older).

In our last annual report, we reported on the analyses using logistic regression and Cox proportional hazards regression models to estimate the odds ratios of late stage disease and mortality for women who were regular users of mammography and women who were non-users. These results form the manuscript submitted and accepted by the Journal of the American Geriatrics Society, a copy of the manuscript is attached.

(6.14) Literature Review

In order to compare our odds ratios and hazards ratios to the data available from the existing randomized clinical trials, we conducted a literature review of all reports in the previous 15 years from both randomized clinical trials, and from case control and cohort studies which addressed mammography use. We reviewed this literature for age specific comparison, which would alllow us to compare the odds ratios estimates for women 65 and older with women 50 – 65 in the clinical trials. We hoped to plot these results along with our own for women 67 – 74 years, 75-84 years, and 85 years and greater. We planned to plot our results with both the adjusted hazards ratio, as well as the adjusted hazards ratio allowing 1.25 years for lead time bias.

Our review of the literature revealed only one report published which stratified the 50 year and older age group into smaller age groupings and found equivalent benefits in 50 – 60 and 60 and older

women. However, with no specific age group overlapping the youngest women in our population, we are unable to complete this analysis to date.

We are in the process of contacting the investigators at each trial, to identify any unpublished estimates of benefit for the women 65 and older separate for the rest of the group. If we are able to identify such estimates, we will complete this planned comparison.

(6.15) Simulated Case-Control Analyses

After review of the recent literature on uses of observational data to address issues of benefit in screening, our research team has developed the following methodology innovative in its application in the field of mammography screening. It combines the recently applied analytic methods of propensity scores and instrumental variable to simulate a case control study using our administrative dataset cohort.

Our decision to develop this methodology grew out the existing literature review and one specific study relevant to our own work. The recent study by Demissie and colleagues (42) compared the results of RCTs with the available data on case control studies measuring the effectiveness of mammography in women 50 – 65 year of age. The authors address the biases in both study designs. One of the major under-estimations of the effectiveness of mammography is due to the cross over between the two groups, with many trials having a substantial number (20 – 30%) of women in the control groups receiving mammography from other sources, and most trials reporting only 50 – 80 % compliance with mammography in the intervention arm. In this paper, they calculated a pooled RRs for women over age 50 of .76 from RCTs compared with .44 from case control studies, which again suggests lead time bias in the case control studies. However, in their calculations of the differences in RRs between the observed data using the intention – to – treat analysis, with adjustment for misclassification based on actual screening behavior, the RRs between the RCT and case control studies narrows considerably. For example, assuming a 70% compliance with mammography in the intervention arm, and 20% mammography in the control arm, an observed RR of .8 would be adjusted to .63, and an observed RR of .7 would be adjusted to .44. The authors conclude "RCTs have measured the effectiveness of mammography in real communities, while the case-control studies have measured efficacy among those women who have actually been screened." This methodology suggests that case control estimates compare favorably with RCT findings, and that a case control methodology is another potential option to address an administrative dataset such as SEER. This led us to pursue case-control methodology.

Growing research in the field of health services research includes using propensity scores and instrumental variables to simulate case-control studies (43). Propensity scores are developed as a measure of the likelihood of each observation within a data set to have the outcome of interest. In our example, using women from the HCFA –SEER database, they are used to determine the likelihood of each woman being a user of mammography.

Our methodology calculates propensity scores based on age, income, use of the health care system (measured as frequency of primary care visits), race, and comorbidities (measured from prior hospitalizations diagnosis in HCFA data). The propensity scores, which is essentially the likelihood of someone being a user based on their measured covariates, will be used to provide equally distributed populations in recognition of lack of measurement of ALL possible risk factors. Those effects of unmeasured risk factors is minimized, if not eliminated, due to the randomization component of this procedure. To develop a propensity score, we first require a model which will accurately predict probability of being a regular user of mammography, using variables associated with likelihood of developing breast cancer. We developed a series of models, including as possible variable patient age, income, number of primary care visits, patient race, and comorbidity. We developed models with and without geographic region, as we plan to analyze region as an instrumental variable. We also considered an interaction term between comorbidity and race, as some data suggests that black women may have fewer prior hospitalization despite significant morbidity, which would bias our morbidity score which is based upon comorbidity assessed during hospitalization.

(6.2 1) Model Development

Our first, or base model (Table A), includes age, income and number of primary care visits as continuous variables, region race and comorbidity as categorical variables. The second model includes the interaction of race and prior hospitalization. The third model addresses age as a categorical variable. Models 4 and 5 exclude region, using age as a continuos and then categorical variable. The findings are that all models accurately predict the likelihood of being a regular user of mammography, with the c statistic of 7.26 and greater in all cases. We currently are refining the model by addressing ages in 5 years age groupings instead of 10 year groups, and categorizing number of primary care visits rather than using this as a continuous variable.

(6.22) Future Analyses

Once we have completed refinements to our model, this final model will be used to determine propensity scores for all subjects within the dataset. Subjects will be divided into quintiles based upon their propensity score (e.g. top 20%, next 20 %, etc.). Once divided into quintiles, within each quintile, we will randomly select equal numbers of users and nonusers, thus providing us with the subset of the cohort to serve as cases and controls for further analyses. With this simulated case control data we will calculate odds ratios and adjusted odds ratios based upon our previously defined potential confounding variables, looking at all women combined, as well as our 3 stratified age groupings. Comparisons between our findings and the literature will be done to determine and quantify bias resulting from our procedures, both to established case-control studies as well as RCTs.

Instrumental variable analysis will also be included in our refinement of our models for the simulated case-control analysis. An instrumental variable is one associated with outcome, but does not affect rates of breast cancer. Region will be considered as an instrumental variable. Region has been shown to be associated with mammography rates [see Table A], but likely does not affect the rates of breast cancer within those who are screened or not screened. Thus, it qualifies as an instrument. Including it as such will allow assessment of effectiveness while accounting for unmeasured risk factors.

(6.3) DISCUSSION

Our results to date have shown a striking association between prior regular mammography use and two outcomes 1) early stage of disease, and 2) breast cancer specific mortality. These data are based on a cohort of nearly 10,000 women over seven years in three geographic regions. Data on diagnosis, stage, mortality and comorbidities are collected prospectively and not subject to recall bias. We have controlled for potential confounders including age, race, income, comorbidities.

The major critique of this observational data is its risk of lead time bias. In the initial analyses, we attempted to adjust for this. Therefore in the last stage of this project, we will attempt to formally calculate lead time bias by comparing our findings for women less than 70 years with the RCT data for this age group.

We continue to work on innovative analytic techniques to address the problem of lead time bias. By utilizing a number of methodologies, all with strengths and limitations in assessing lead time bias, we hope to demonstrate whether a broad range of methodologies all point to the benefit on screening mammography in older women.

(6.4) STATEMENT OF WORK

We have met the following objectives for the third 12 months of the project.

Table A

	95% Confidence Intervals on Odds Ratios for Predicting Users (n=2560)vs. Non-Users (n=2320)				
			MODEL		
	1: base	*2: interaction*	*3: age cat*	*4: no region*	*5: age cat/no reg*
Age	**0.918, 0.937**	**0.918, 0.937**		**0.917, 0.936**	
85+			**0.144, 0.229**		**0.145, 0.230**
75-84			**0.604, 0.789**		**0.598, 0.779**
-74 (ref)			(1.000)		(1.000)
Income (10k)	0.956, 1.047	0.956, 1.048	0.960, 1.052	0.905, 0.979	0.906, 0.980
Region					
Seattle	**1.341, 1.864**	**1.342, 1.866**	**1.372, 1.909**		
Atlanta	**0.608, 0.874**	**0.607, 0.873**	**0.614, 0.882**		
Conn (ref)	(1.000)	(1.000)	(1.000)		
PCVisits	**65.150, 382.451**	**65.196, 382.716**	**64.212, 376.739**	**64.730, 379.617**	**63.899, 374.521**
Black	**0.419, 0.791**	**0.356, 0.766**	**0.432, 0.813**	**0.294, 0.539**	**0.300, 0.549**
Comorbidity					
NotHosp (ref)	(1.000)	(1.000)	(1.000)	(1.000)	(1.000)
NoHosps	0.950, 1.280	0.961, 1.303	0.955, 1.287	0.906, 1.215	0.909, 1.219
SomeHosp	**0.563, 0.809**	**0.570, 0.826**	**0.565, 0.814**	**0.533, 0.764**	**0.534, 0.766**
Blknhosp		0.712, 2.521			
c-stat	0.742	0.742	0.742	0.726	0.727

Model 1: The base model that was used
Model 2: Including an interaction between race and comorbidity.
Model 3: Using age categories (10 years) instead of the continuous variable.
Model 4: Excluding region.
Model 5: Excluding region AND using age categories.

Technical Objective 4:

Task 2 Completed analyses to describe relationship between prior mammography use and survival for each age.

Technical Objective 5:

Task 1 Conducted literature review to identify results form RCTs stratified within the age 50 and older category.

Task 3 We have presented our findings to date at the Era of Hope Department of Defense Breast Cancer Research Program meeting June 8 – 11, 2000.
We have completed our first manuscript, which is in press for publication at the Journal of the American Geriatrics Society.

We will continue to address the following objectives during the permitted no-cost extension period of the grant.

Task 1 Contact RCTs investigators for unpublished data on estimates stratified by age 50 – 65 and 65 and older.

Task 2 Develop and complete analyses using propensity scores and operational variables.

(7) KEY RESEARCH ACCOMPLISHMENTS

1. Oral presentation to the Era of Hope Meeting.
2. Manuscript accepted for publication to the Journal of the American Geriatrics Society.
3. Developed innovative methodology using propensity scores.

(8) REPORTABLE OUTCOMES

1. Manuscript accepted for publication to the Journal of the American Geriatrics Society.

(9) CONCLUSIONS

Our data are the first to demonstrate a benefit in mammography in women over age 70 years. The final phase of the study will attempt to assess the degree of lead-time bias in this data by comparing are results with data for 65 – 70 year old women in the RCTs. This analysis should eliminate the concerns of lead time bias in the use of this database, and provide the ability to make estimates of the effectiveness of mammography in women over age 70 years.

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MAMMOGRAPHY USE, BREAST CANCER STAGE AT DIAGNOSIS, AND SURVIVAL AMONG OLDER WOMEN

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ABSTRACT

Background: Women age 65 years and older account for most newly diagnosed breast cancers and deaths from breast cancer. Yet, older women are least likely to undergo mammography, perhaps because mammography's value is less well demonstrated in older women.

Objective: To investigate the relationship between prior mammography use, cancer stage at diagnosis, and breast cancer mortality among older women with breast cancer.

Design: Retrospective cohort study using the Linked Medicare-Tumor Registry Database.

Setting: Population-based data from three geographic areas included in the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program.

Participants: Women aged 67 and older diagnosed with a first primary breast cancer, from 1987 to 1993, residing in Connecticut, metropolitan Atlanta, Georgia, or Seattle-Puget Sound, Washington.

Measurements: Medicare claims were reviewed and women were classified according to their mammography use during the 2 years before diagnosis: nonusers (no prior mammograms), regular users (at least 2 mammograms at least 10 months apart), or peri-diagnosis users (only mammogram(s) within 3 months before diagnosis). Mammography utilization was linked with SEER data to determine stage at diagnosis and cause of death. Our main outcome variables were

1) stage at diagnosis, classified as early (in situ/Stage I) or late (Stage II or greater), and 2) breast cancer mortality, measured from diagnosis until death from breast cancer or end of the follow-up period (December 31, 1994).

Results: Older women who were nonusers of mammography were diagnosed with breast cancer at Stage II or greater more often than regular users (adjusted odds ratio (OR), 3.12 [95% CI, 2.74-3.58]). This association was present within each age group studied. Nonusers of mammography were at significantly greater risk of dying from their breast cancer than regular users for all women (adjusted hazard ratio (HR), 3.38 [95% CI, 2.65-4.32]) and for women within each age group. Even assuming a lead time of 1.25 years, nonusers of mammography continued to be at increased risk of dying from breast cancer. Our findings remained significant for all women and for the two youngest age groups (67 to 74 years, 75 to 85 years), although the benefit was no longer statistically significant for the oldest women (85 years and older).

Conclusion: Older women who undergo regular mammography are diagnosed with an earlier stage of disease and are less likely to die from their disease. These data support the use of regular mammography in older women and suggest that mammography can reduce breast cancer mortality in older women, even for women age 85 and older.

INTRODUCTION

Breast cancer is an important public health problem in the United States, particularly among older women (age 65 years and older). Each year, more than 180,000 American women develop breast cancer and more than 40,000 die from the disease.[1] Older women bear the greatest burden of disease because the risks of developing and dying from breast cancer rise sharply with advancing age.[2] The National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results (SEER) Program reports that older women account for 48% of newly diagnosed invasive breast cancers and 58% of breast cancer deaths.[3] The SEER Program also documents a 12% increase in the breast cancer mortality rate in older women from 1973 to 1994, despite a decline in overall rate.[3] This may be partially due to the fact that older women are more likely to present with advanced breast cancer at diagnosis,[2,4-6] possibly because they are less likely to undergo regular mammography.[7]

Early detection with mammography has been shown to reduce breast cancer mortality by 20 to 39% in women aged 50 to 69 years.[8-12] Despite this striking reduction in mortality, it is unknown whether mammography continues to be useful beyond age 70 or at what age, if any, breast cancer screening and early detection is no longer of value.[13] Unfortunately, none of the randomized controlled mammography trials included women over 74 years of age. Although one mammography trial (the Swedish Two County Trial) included women up to age 74 years, there was inadequate power to establish a mortality reduction specifically for women over age 69 years.[12] Therefore, breast cancer screening guidelines for the elderly are based on extrapolating data from women under age 70 and mammography recommendations vary.

Without clear scientific evidence, older women and their physicians are left to make decisions on an individual basis. Since it is unlikely that a randomized controlled trial will ever be implemented in women over age 70, conclusions about the value of mammography in the elderly will most likely be inferred from observational studies, such as the one reported here. Therefore, we sought to improve our understanding of the relationship between previous mammography use and 1) cancer stage at diagnosis, and 2) breast cancer mortality among older women diagnosed with breast cancer in NCI's SEER Program.

METHODS

Data Source

We conducted a retrospective cohort study using the Linked Medicare-Tumor Registry Database.[14] The linked database was jointly created by the National Cancer Institute (NCI) and the Health Care Financing Administration (HCFA) to enable researchers to conduct cancer-related health services research. The linked database contains cancer information on patients 65 years of age and older from NCI's SEER Program and Medicare enrollment and utilization information from HCFA's Medicare Statistical System. The linked database contains Medicare data from 1985 to 1994 for breast cancer cases diagnosed between 1973 and 1993.

Two Medicare utilization files are included in the linked database. First is the Medical Provider Analysis and Review (MEDPAR) file, which is a 100 percent utilization file with one record for every inpatient hospitalization or skilled nursing facility stay covered under Medicare Part A. Second is the Physicians' Claims file which is a 100 percent utilization file with one record for every physician claim covered under Medicare Part B. Before 1991, the 100 percent Physicians' Claims file was available for only ten states. Therefore, for our study years, 1987 to 1993, data from the SEER and Medicare Programs overlap in tumor registries for three areas: Connecticut, metropolitan Atlanta, Georgia, and Seattle-Puget Sound, Washington. Specific information describing the linkage between SEER and Medicare has been published elsewhere.[14] The match rates for Connecticut, Atlanta, and Seattle were 93.3%, 94.1%, and 91.5%, respectively.

Study Sample

Women were eligible for the study sample (n=11,399) if they received a first primary diagnosis of breast cancer between 1 January 1987 and 31 December 1993, were 67 years of age or older, and resided in Connecticut, Atlanta, or Seattle-Puget Sound. Although we selected these areas because physicians' claims were available for all cases, they also represent a geographically diverse population of older women with breast cancer. Women who were enrolled in a health maintenance organization and those with less than two full years of Medicare Part B coverage were not eligible for this study, since their physician claims data (which are required for identifying mammography use) were not available. We restricted our final study sample to women who were 67 years of age and older to ensure that all women had a full two years of Medicare utilization (claims) information before their breast cancer was diagnosed.

Measures

We ascertained the following sociodemographic information from SEER: age at diagnosis, marital status, and SEER area. Age at diagnosis (range, 67-107 years) was categorized as 67 to 74, 75 to 84, and 85 and older. Marital status was defined as married or not at diagnosis. SEER area was classified according to the tumor registry of diagnosis: Connecticut, Atlanta, or Seattle. We used 1990 U.S. Census data to define an ecological measure of socioeconomic status: women were assigned to the median household income of their zip code of residence and grouped as $<$ \$25,000 or $\geq$ \$25,000.

We obtained information on race from the Medicare beneficiary enrollment file. Enrollees are classified in Medicare files as Black, White, Asian, Native American, Hispanic, or unspecified.

We grouped women who were of racial/ethnic backgrounds other than Black or White together because there were too few women to permit separate analyses.

We computed a modified Charlson Comorbidity Index using Deyo's method of classifying ICD-9-CM *(International Classification of Diseases, 9th revision, Clinical Modification)* diagnosis codes from inpatient claims.[15] For each woman, we identified all inpatient hospitalizations beginning two years prior to diagnosis and ending one month after diagnosis. A priori, we extended the observation period to one month past diagnosis because we expected women to have at least one hospitalization around the time of diagnosis. We classified women as 1) non-hospitalized (i.e., comorbidity could not be assessed), 2) having no comorbid conditions (Charlson Index of 0), or 3) having one or more comorbid conditions (Charlson Index $\geq$ 1).

We measured mammography utilization using Medicare physicians' claims. We identified all bilateral mammograms [CPT *(Physicians' Current Procedural Terminology)* procedure codes 76091 *(mammography, bilateral)* or 76092 *(screening mammography, bilateral, two films each breast)*] within two years prior to the breast cancer diagnosis. We classified women as 1) *nonusers* (n=2,029) if they had no mammograms during the entire two year period prior to diagnosis, 2) *regular users* (n=2,383) if they had at least two mammograms within the two years prior to their breast cancer diagnosis that were ten or more months apart, and 3) *peri-diagnosis users* (n=5,355) if they had their only mammogram(s) within three months before diagnosis. The peri-diagnosis users were a heterogeneous group of women whose only mammography use was close to their breast cancer diagnosis. This group includes women who had a screening mammogram which led to their breast cancer diagnosis and those whose mammograms were

diagnostic. Therefore, analyses relating prior mammography use to breast cancer outcomes considered only nonusers and regular users, as they are clearly distinct groups.

Our first outcome was stage at diagnosis. We measured cancer stage using the TNM (tumor, node, metastases) staging system adopted by the American Joint Committee on Cancer. We categorized late-stage disease using two classification schemes. First, women diagnosed with carcinoma in situ or Stage I tumors were classified as early-stage; those diagnosed with Stage II or greater tumors were classified as having late-stage disease. Second, we restricted late-stage disease to include only women diagnosed with Stage IIB or greater; women diagnosed with Stage IIA were reclassified as having had early-stage disease. We repeated our analyses using both classification systems and obtained similar results. We present our analyses classifying late-stage disease as Stage II or greater because they provide a more conservative estimate of the mammography-stage association.

Our second outcome was breast cancer mortality among women with invasive tumors. Women who had carcinoma in situ (n=479) were excluded from this analysis because it is unknown which tumors will progress to invasive disease. We measured survival time as the number of days from date of diagnosis until date of death or 31 December 1994 (end of follow-up). Date of death was obtained from the 1994 Medicare beneficiary enrollment file. Cause of death, obtained from SEER, captures the underlying cause listed on the death certificate. Women who had ICD-O *(International Classification of Diseases, Oncology)* codes 174.8 and 174.9 were classified as having died from breast cancer.

Women whose mammography use could not be categorized (788 women) or whose disease was unstaged (844 women) were excluded from the study. Overall, there were 741

women age 67 to 74 years, 620 women 75 to 84 years, and 271 women 85 and older who met these exclusion criteria.

Follow-up for our final sample (n=9,767) ranged from one to eight years depending on the year of diagnosis. By the end of 1994, 2,332 deaths had occurred; 889 deaths were attributed to breast cancer (385 women 67 to 74 years, 390 women 75 to 84 years, and 114 women 85 years and older).

Statistical Analysis

All statistical analyses were performed using SAS statistical software version 6.12.[16] We performed each analysis once for all women and again for women within each age group. We compared women across age groups with respect to sociodemographic factors, comorbidity, stage at diagnosis, and prior mammography use. Chi-square statistics and Students' t-tests were used to identify characteristics at diagnosis that varied significantly with age at diagnosis.

Multivariable logistic regression was used to estimate crude and adjusted odds of late-stage disease for women who failed to undergo mammography compared with women who used regular mammography.[17] The odds ratio (OR) for prior mammography use and the corresponding 95 percent confidence intervals (CI) were estimated from the β coefficient and standard error from the logistic models.[17] Multivariable logistic models adjusted for factors previously found to be related to stage at diagnosis including age at diagnosis, race, marital status, income of zip code of residence, and comorbid conditions.[18] For models fit to each age group, we adjusted for age at diagnosis as a continuous variable to account for any residual confounding with age.

To better understand overall survival (i.e., death from all causes) in our study sample, we computed Kaplan-Meier estimates of 5-year survival by age group for each stage at diagnosis.

We combined women with Stage III and IV disease to have sufficient numbers for meaningful analysis. Since this analysis describes survival regardless of cause of death, only women who were alive at the end of follow-up were censored. The Log-rank test was used to identify differences in overall survival by age group within each stage stratum.[19]

To further examine the relationship of mammography use and survival, we hypothesize that mammography use should primarily affect breast cancer-related deaths. Therefore, we fit stratified Cox proportional hazards regression models to estimate the crude and adjusted risk of death from breast cancer for women who failed to undergo mammography compared with women who used mammography regularly. All models were stratified by SEER area to account for any lack of proportionality among the three tumor registries by allowing the underlying hazard to differ. In these analyses, women were also censored when they died from causes other than their breast cancer. Each hazard ratio (HR) (i.e., relative risk of mortality) for prior mammography use and its corresponding 95 percent CI was estimated from the β coefficient and standard error from a Cox model.[19]

Analyses of post-diagnosis survival in relation to cancer screening are subject to lead time bias in which a woman whose disease is diagnosed earlier through screening will live longer "following diagnosis" simply due to earlier detection. Unfortunately, we do not know any individual's lead time or which women had tumors diagnosed clinically or through screening. We explored the potential effect of lead time bias on our survival results by estimating the risk of dying from breast cancer for nonusers compared with regular users after allowing for a lead time of 1.25 years for each regular user. The number 1.25 years is approximately one-half the mean

sojourn time (i.e., on average the maximum lead time achievable) for women 70 to 74 years in the Swedish Two County Trial.[20]

RESULTS

Characteristics of the study sample (n=9,767) are presented by age group at diagnosis in Table 1. Overall, 47% of women were aged 67 to 74 years at the time of their breast cancer diagnosis, 42% were 75 to 84 years, and 11% were 85 years or older.

Overall, 21% of women had no mammograms within two years prior to their breast cancer diagnosis (nonusers), 24% of women had at least two mammograms within two years preceding diagnosis that were ten or more months apart (regular users), and 55% had their only mammogram(s) within three months prior to their diagnosis (peri-diagnosis users). Figure 1 presents the percentage of women who were nonusers and regular users of mammography according to age at diagnosis. The proportion of women who were peri-diagnosis users was similar across the age groups and is not displayed. Regular mammography use decreased with advancing age at diagnosis such that the women in the oldest age group were substantially less likely to undergo regular mammograms: 29% of women 67 to 74 years, 23% of women 75 to 84 years, and 10% of women 85 years or older were regular users. Although in the two youngest age groups, the proportion of nonusers was similar (18% of women 67 to 74 years and 21% of women 75 to 84 years) and less than the proportion of regular users, the reverse was true for the oldest women. One-third of women 85 years and older did not undergo mammography within two years before their diagnosis.

Figure 2 presents the distribution of stage at diagnosis according to age at diagnosis. Within each age group, most women presented with Stage I or Stage II breast cancers. The distribution of disease among women in the two younger groups is nearly identical, except that fewer women 75 to 84 years presented with carcinoma in situ compared with women 67 to 74

years (8% versus 12%, respectively). However, there is a noticeable shift in the distribution of disease among the oldest women, characterized by the greater frequency of Stage II and Stage III cancers diagnosed in women 85 years and older. Late-stage (i.e., Stage II or greater) breast cancer was diagnosed in 41% and 45% of women 67 to 74 years and 75 to 84 years, respectively, and in 53% of women 85 years or older.

Figure 3 presents the percentage of nonusers and regular users of mammography who were diagnosed with late-stage disease for each age group. Within each age group, nonusers were significantly more likely to be diagnosed with late-stage disease than regular users. Furthermore, the proportion of nonusers who were diagnosed with late-stage disease increased with advancing age (49% aged 67 to 74 years, 60% aged 75 to 84 years, and 69% aged 85 years or older). In contrast, the proportion of regular users who presented with late-stage disease at diagnosis was substantially lower (28%) and was similar across age groups.

Table 2 presents the odds ratios for late-stage disease comparing nonusers with regular users of mammography for all women and for each age group separately. These analyses were performed to determine whether the relation between prior mammography use and stage at diagnosis is significant for older women of different age groups. Prior mammography use was strongly associated with stage at diagnosis for all women and women in each age group. Even after adjusting for factors that have been found to be associated with late-stage disease at diagnosis, including age at diagnosis, race, marital status, income of zip code of residence, and comorbid conditions, lack of mammography use remained a significant predictor of late-stage at diagnosis in all women (adjusted OR, 3.12 [95% CI, 2.74-3.58]) and within each age group: 67

to 74 years (adjusted OR, 2.46 [95% CI, 2.04-2.98]); 75 to 84 years (adjusted OR, 3.64 [95% CI, 2.96-4.48]); and 85 years or older (adjusted OR, 6.87 [95% CI, 3.97-11.90]).

Table 3 presents overall 5-year survival estimates (i.e., deaths from all causes) following diagnosis by stage at diagnosis and age group. Survival decreased with later stage at diagnosis. Furthermore, survival decreased steadily with advancing age within each cancer stage.

Table 4 presents the hazard ratios for breast cancer mortality, comparing nonusers with regular users of mammography for all women and for each age group separately. Table 4 also presents results demonstrating the potential effect of a lead time of 1.25 years. The results in Table 4 focus on breast cancer mortality because one would expect that mammography would primarily impact on deaths from breast cancer. After adjusting for sociodemographic factors and comorbidity, nonusers were at significantly greater risk of death from breast cancer than regular users and had greater risk of dying from breast cancer within each age group. Consideration of lead time somewhat diminished the magnitude of the hazard ratio, but nonusers of mammography continued to be at increased risk of dying from breast cancer. Our findings remained significant for all women and for the two youngest age groups. Although the point estimate remained increased for the oldest women, it no longer achieved statistical significance.

DISCUSSION

In the absence of data on older women from randomized controlled trials, we sought to improve our understanding of the relationship between prior mammography use and breast cancer outcomes in older women. We found that women with breast cancer aged 67 years and older were significantly more likely to be diagnosed with Stage II or greater disease if they were nonusers of mammography than if they were regular users. Women who were nonusers of mammography were also at greater risk of dying from their breast cancer than those who were regular users. Most importantly, these findings persist with advancing age at diagnosis.

We have shown that regular mammography use is associated with earlier diagnosis of breast cancer in older women. In fact, within each age group studied, we found that in situ and Stage I cancers were more common among regular users and that the proportion of women who presented with Stage II or greater disease was substantially lower for regular users than for nonusers. Two studies have demonstrated similar results. A case-control study of older women conducted in the United States suggested an association between screening mammography and a reduction in metastatic breast cancer, but lacked sufficient power to demonstrate significance.[21] Faulk and coworkers examined the clinical efficacy of mammography among women aged 65 years and older compared with women aged 50 to 64 years and found that mammography was at least as effective in detecting breast cancers with a favorable prognosis in older women on several measures. They found that mammography detected slightly smaller tumors in older women, that were more often axillary node negative, and in an earlier stage.[22]

Even though reduced breast cancer mortality is the ultimate goal of breast cancer screening, some have argued that intermediate measures, such as stage at diagnosis, are useful for

evaluating the utility of screening.[23] Our data demonstrate a significant reduction in Stage II or greater tumors among women who were regular mammography users. It is well established that stage at diagnosis is the most important predictor of survival and that stage is inversely correlated with survival. Therefore, these results suggest that regular users should have a more favorable prognosis because they are diagnosed earlier in the disease process. Previously, the Swedish Two Country Trial demonstrated that a 25% reduction in advanced staged breast cancers for screened women translated to a 30% reduction in breast cancer mortality.[24]

Indeed we found a consistent lower risk of death from breast cancer among regular users of mammography overall and within each age group. Few other studies have examined the relationship between mammography utilization and breast cancer mortality for older women, and most have relied on observational data. The only randomized study to offer insight into screening for women aged 70 to 74 years is the Swedish-Two County trial, which showed a persistent 34% reduction in breast cancer mortality for women 50 to 74 years after 13 years of follow-up.[20] Although poor compliance precluded age-specific mortality analyses for women over age 70,[1] more than half of the women over age 70 who died of breast cancer were among those who had refused screening.[25] A follow-up study of women in the Breast Cancer Detection Demonstration Project found that the observed number of breast cancer deaths among women aged 60 to 74 years was 26% less than the expected based on national data.[26] Case-control studies in the Netherlands have also evaluated the efficacy of screening mammography in older women by comparing a population-based screening program in Nijmegen to a neighboring city without a formal screening program. Although initial analyses suggested a modest effect of

mammography,[27,28] a recent analysis estimated that regular mammography reduced breast cancer mortality in older women by approximately 45%.[29]

Although Medicare claims data have been used effectively to measure mammography,[7,18,30-32] there are some potential limitations. First, our study is limited to women enrolled in fee-for-service settings as Medicare data do not capture services rendered to HMO enrollees. Few women were enrolled in managed care during our study years, however, the proportion of Medicare HMO enrollees increased from 4% to 13% between 1990 and 1997.[14,33]

Second, Medicare reimbursement policies have changed over time. Medicare began reimbursing providers for biennial screening mammography in 1991 and annual screening mammography in 1998. Although Medicare only paid for diagnostic mammograms prior to 1991, studies show that providers were performing screening mammograms and billing Medicare under the diagnostic procedure code both before and after the change in reimbursement.[7,30-32] Nevertheless, we cannot determine whether an individual mammogram was done for screening or diagnostic purposes. To address this issue, we examined how women used mammography over time. We defined our measure of mammography use to identify two distinct groups: 1) women who had no evidence of mammography use during the two years before diagnosis, and 2) those who demonstrated a pattern of regular use by having had at least two mammograms that were at least 10 months apart. We selected 10 months as a clinically reasonable interval to assume that women were undergoing screening and were not being followed for a suspicious lump. Although women with a pattern of regular use seemed to be using mammography for screening, we do not know which women had their cancer detected by symptoms and confirmed with diagnostic mammography.

Due to the observational nature of this study, three potential sources for bias inherent to evaluations of cancer screening must considered. These sources of bias are over-detection, length time, and lead time.[34] Over-detection bias occurs when screening detects potentially clinically insignificant tumors. To address this issue, we approached our survival analyses conservatively by excluding women diagnosed with carcinoma in situ to minimize the potential affect of over-detection bias.

Length time bias occurs when the underlying tumor growth rate differs between screened and unscreened groups such that slow-growing less aggressive tumors are more likely to be detected with screening and fast-growing aggressive tumors are more likely to be detected clinically. For this reason, length time bias is of particular concern in studies that include prevalent cancers found on initial screening examinations. Length time bias is less of a concern in our study for two reasons. First, our sample consisted of women with incident breast cancer. Second, older women generally have less aggressive tumors than younger women.[35] We have only limited information on tumor characteristics. However, regular users and nonusers appear similar with respect to pathologic grade; only 18% of regular users and 20% of nonusers had poor or undifferentiated tumors.

As mentioned previously, lead time bias artificially extends the survival time of screened women by advancing the date of diagnosis and is the primary methodologic limitation to using post-diagnosis survival as an outcome of cancer screening. Since we do not know any individual's lead time or who had their tumors diagnosed clinically or through screening, we sought to explore the potential effect of lead time bias on our survival results by allowing for a lead time of 1.25 years for each regular user.[20] We found that adjustment for lead time diminished

the magnitude of the hazard ratio, but that nonusers of mammography continued to be at increased risk of dying from breast cancer. Our findings remained significant for all women and for the two youngest age groups. However, for the oldest women, the point estimate for the hazard ratio remained increased, but the confidence limits included unity -- possibly due to the fewer women in this age group.

Finally, it is important to note the following limitations when interpreting our breast cancer mortality results. First, follow-up for our study sample ranged from one to eight years. It is unknown whether the mortality difference that we observed between nonusers and regular users would persist with additional years of follow-up. Second, although we considered the effect of lead time using an estimate of 1.25 years based on data for women aged 70 to 74 years,[20] it is possible that lead time may be longer. Unfortunately, we do not have enough follow-up to examine longer lead time estimates.

In summary, this study describes the relationship between prior mammography use, cancer stage at diagnosis, and breast cancer mortality. Our data suggest that women who fail to undergo mammography are more often diagnosed with Stage II or greater breast cancer and are at increased risk of dying from breast cancer. Moreover, breast cancer was an important cause of death; breast cancer was the cause in 38% of all deaths in our study sample. These data support the use of regular mammography in older women and suggest that mammography can reduce breast cancer mortality for older women, even for women age 85 and older.

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Table 1. Characteristics of the Study Sample by Age at Diagnosis

	Age at Diagnosis			
	67 to 74 (n=4,609)	75 to 84 (n=4,072)	≥ 85 (n=1,086)	Total (n=9,767)
	n (%)	n (%)	n (%)	n (%)
SEER Area*				
Connecticut	2110 (46)	1992 (49)	536 (50)	4638 (48)
Seattle	1687 (37)	1392 (34)	384 (35)	3463 (35)
Atlanta	812 (17)	688 (17)	166 (15)	1666 (17)
Race				
White	4236 (92)	3785 (93)	1020 (94)	9041 (93)
Black	208 (4)	178 (4)	38 (3)	424 (4)
Other	165 (4)	109 (3)	28 (3)	302 (3)
Married at Diagnosis†				
No	2251 (49)	2803 (69)	975 (90)	6029 (62)
Yes	2358 (51)	1269 (31)	111 (10)	3738 (38)
Median Income of Zip Code				
≥ $25,000	4158 (91)	3678 (91)	976 (90)	8812 (91)
< $25,000	432 (9)	386 (9)	107 (10)	925 (9)

	Age at Diagnosis			
	67 to 74	75 to 84	≥ 85	Total
	(n=4,609)	(n=4,072)	(n=1,086)	(n=9,767)
	n (%)	n (%)	n (%)	n (%)
Comorbidity[†]				
Non-hospitalized	1174 (25)	1001 (25)	298 (27)	2473 (25)
0	2559 (56)	2126 (52)	460 (42)	5145 (53)
1	627 (14)	640 (16)	224 (21)	1491 (15)
≥ 2	249 (5)	305 (7)	104 (10)	658 (7)

[*]$p = 0.018$.

[†]$p < 0.001$.

Table 2. Crude and Adjusted Odds Ratios for Late Stage Disease

Nonusers Compared with Regular Users (n = 4,412)

	Stage ≥ II at Diagnosis	
	Crude	**Adjusted***
	OR (95% CI)	**OR (95% CI)**
All Women (n=4412)	3.36 (2.96-3.81)	3.12 (2.74-3.58)
Age 67 to 74 (n=2167)	2.43 (2.03-2.92)	2.46 (2.04-2.98)
Age 75 to 84 (n=1790)	3.74 (3.07-4.55)	3.64 (2.96-4.48)
Age ≥ 85 (n=455)	6.25 (3.86-10.12)	6.87 (3.97-11.90)

*Adjusted for age at diagnosis as a continuous variable, race, marital status, income of ZIP Code, and comorbidity.

Table 3. Relation of Stage at Diagnosis to Five-Year Survival Estimates By Age at Diagnosis Among Nonusers and Regular Users Combined (n = 3,933)*

Stage at Diagnosis and Age	n	5-year Estimated Survival (SE)	Log Rank P-value†
Stage I			
67 to 74	1083	0.877 (0.013)	
75 to 84	856	0.842 (0.016)	
≥ 85	168	0.496 (0.052)	0.0001
Stage II			
67 to 74	567	0.785 (0.021)	
75 to 84	535	0.620 (0.026)	
≥ 85	185	0.345 (0.043)	0.0001
Stage III/IV			
67 to 74	217	0.362 (0.040)	
75 to 84	238	0.286 (0.036)	
≥ 85	84	0.225 (0.055)	0.039

* Women with carcinoma in situ were excluded from these analyses.

†Log Rank tests differences in overall survival by age at diagnosis.

Table 4. Crude and Adjusted Risk of Breast Cancer Mortality by Age at Diagnosis

Nonusers Compared with Regular Users (n = 3,933)*

	Breast Cancer Mortality			
	From the Date of Diagnosis		Assuming a Lead Time of 1.25 Years for Regular Users	
	Crude	Adjusted†	Crude	Adjusted†
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
All Women (n=3933)	3.53 (2.80-4.45)	3.38 (2.65-4.32)	2.36 (1.87-2.98)	2.28 (1.79-2.91)
Age 67 to 74 (n=1867)	3.18 (2.27-4.46)	2.94 (2.08-4.17)	2.14 (1.52-3.01)	2.14 (1.51-3.02)
Age 75 to 84 (n=1627)	3.69 (2.58-5.27)	3.95 (2.72-5.74)	2.41 (1.68-3.46)	2.47 (1.70-3.58)
Age ≥ 85 (n=437)	2.71 (1.22-6.04)	2.29 (1.00-5.26)	1.74 (0.78-3.90)	1.45 (0.63-3.32)

* Women with carcinoma in situ were excluded from these analyses.

†Adjusted for age at diagnosis as a continuous variable, race, marital status, income of ZIP Code, comorbidity, and year of diagnosis. Proportional Hazards models were stratified on SEER area.

‡Hazard ratio (95% confidence interval).

Figure 1. Prior Mammography Use By Age at Diagnosis

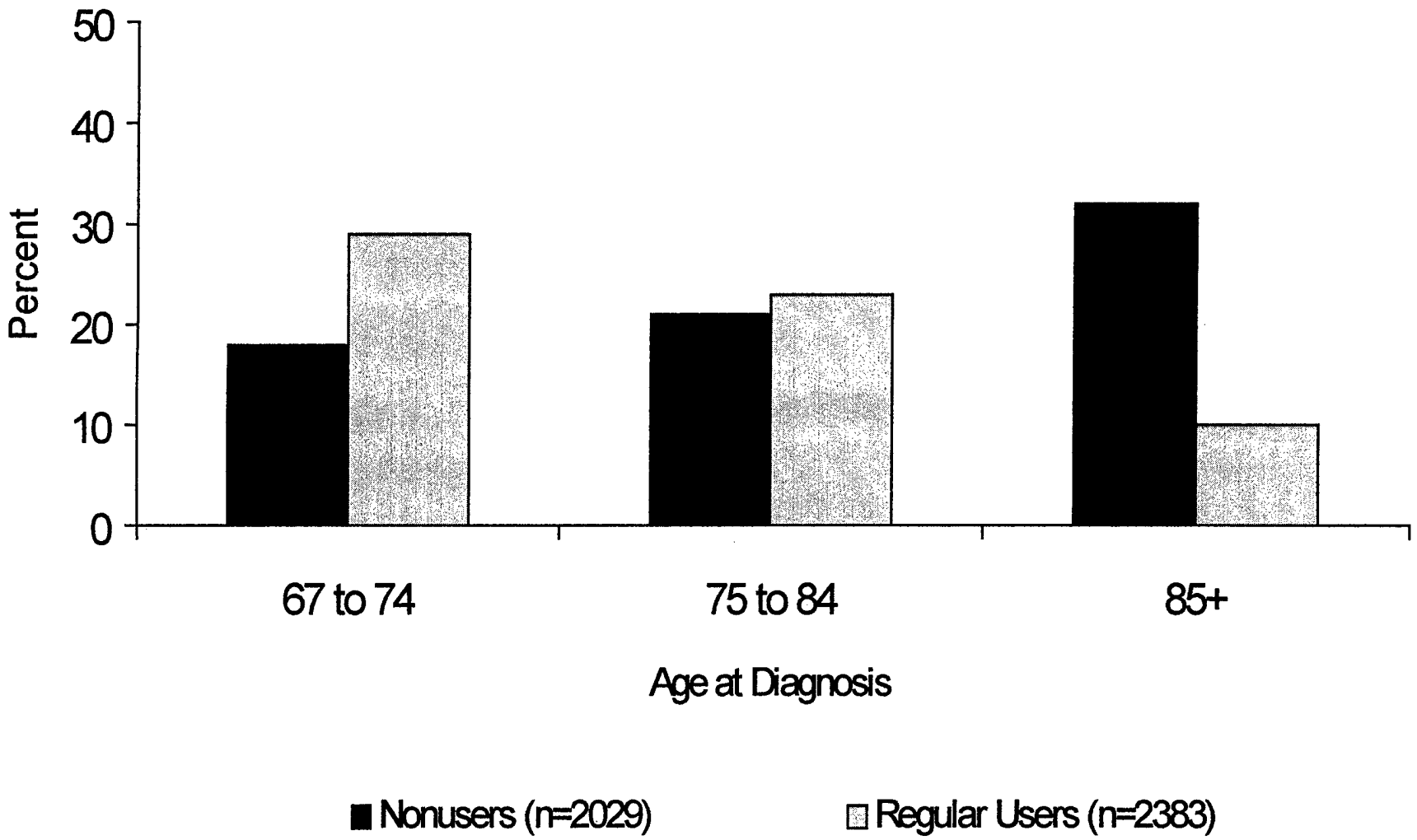

Figure 2. Stage at Diagnosis By Age at Diagnosis

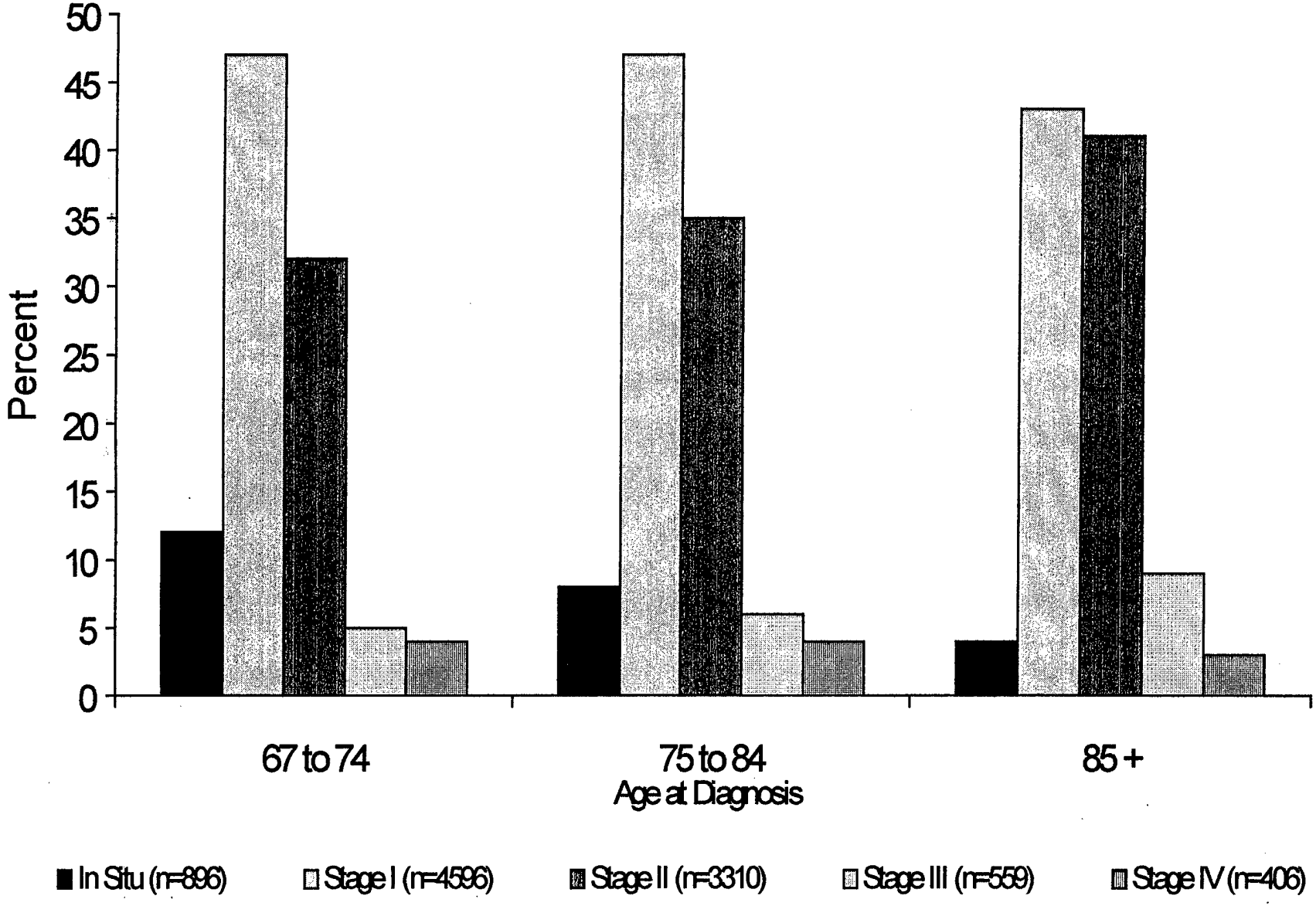

Figure 3. Percentage of Women with Stage ≥ II Disease By Prior Mammography Use and Age at Diagnosis